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TOXIC amblyopia is an ocular condition, characterized by dimness of vision and an alteration of the color fields, the etiological factor being, in most cases, a substance of exogenous origin.

In his discussion of toxic amblyopia due to carbon bisulphide intoxication, Knapp [1] states:

> . . . the patients complain of seeing through a cloud; there is the characteristic central disturbance of vision with a comparatively free periphery of the field and the loss of color perception in the center. The condition is usually bilateral and all the reports agree on the presence of the central defect with normal periphery of the field, characteristic for toxic amblyopia in general.

In the present study of toxic amblyopia due to carbon tetrachloride poisoning, perimetric examination revealed no central defect but a marked constriction of the periphery of the visual color fields. The subjective symptom of dimness of vision, however, was the same as in the usual toxic amblyopia as typified by carbon bisulphide poisoning.

OBSERVATION OF CASES

Five adult male workers from four establishments in the dry cleaning industry were examined. All of these men were exposed to carbon tetrachloride vapor from 8 to 10 hours daily for periods varying from 1 to 6 months preceding examination.

Case 1—J. L., a white male, age 20, had been exposed for a period of 5 weeks previous to examination. He complained chiefly of severe frontal headache associated with vertigo, tinnitus, nausea and vomiting. He was unable to eat without subsequently vomiting most of the ingested food. These symptoms started within a few days after commencing this work. About 3 weeks after exposure began, he noticed a gradually increasing disturbance of vision, manifested by seeing "spots before the eyes." He also complained of a marked disturbance of the sense of taste, so that "even cigarettes tasted like bile." Physical examination revealed a well developed white male, weight 218 lb., appearing somewhat lethargic and stuporous. There was moderate pallor of his skin. The sclerae had a slight icteric tinge. The pupils were normal and reacted normally to light and accommodation. Heart and lungs were normal. Abdominal examination was normal. Reflexes were physiological. Blood sugar tolerance analyses were as follows:

	Blood Sugar	*Urine Sugar*
Fasting	87 mg.	Slight
30 Min.	154 mg.	None
1 Hr.	115 mg.	Trace
2 Hr.	99 mg.	None
3 Hr.	90 mg.	None

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Case 2—F. K., a white male, age 43, had been exposed to the carbon tetrachloride vapors for a period of 10 weeks previous to examination. Before the period of exposure he had been in good health. Since working at the dry cleaning plant, he had had continual nausea but did not vomit. The nausea was accompanied by marked dizziness, headache, and weakness. He suffered no pain of any kind. About 2 weeks after commencing work, his vision became blurred and his eyes felt greatly irritated. In addition to the above complaints, there was marked polyuria and constipation. Physical examination showed a well developed white male, weight 165 lb., appearing somewhat weak and lethargic. The conjunctivae were congested and there was marked epiphora. Heart was normal. They were a few moist râles at both lung bases. The abdomen was normal. Reflexes were normal. Blood sugar tolerance analyses were as follows:

	Blood Sugar	*Urine Sugar*
Fasting	90 mg.	Slight
30 Min.	169 mg.	Moderate
1 Hr.	150 mg.	Large Amt.
2 Hr.	84 mg.	Mod.
3 Hr.	61 mg.	Slight

Case 3—H. M., a white male, age 30, had been exposed for a period of 4 weeks previous to examination. During this period he had severe diarrhea with moderate abdominal pain. Two weeks after the onset of the exposure nausea and vomiting began. The vomiting occurred about 15 minutes after each meal, being most marked after the noonday meal. In the period after the onset of the gastric symptoms he lost 6 lb. in weight. He complained of increasing muscular weakness and lassitude. Physical examination revealed a well developed white male, weight 146 lb., appearing markedly irritable. There was marked skin palor. The conjunctivae were congested and there was marked epiphora. Heart, lungs and abdomen were normal. There was slight exaggeration of the abdominal reflexes and also a slight tremor of the hands. Blood sugar tolerance analyses were as follows:

	Blood Sugar	*Urine Sugar*
Fasting	90 mg.	Slight
30 Min.	118 mg.	None
1 Hr.	95 mg.	Slight
2 Hr.	89 mg.	Slight
3 Hr.	80 mg.	Slight

Case 4—R. V., a white male, age 48, had been exposed for a period of 6 months before examination. He complained of severe dizziness, headache, nausea, and vomiting. The ocular symptoms in this case were more marked than in any of the others. He stated that everything looked smaller than previously; that he had black spots before his eyes continually. The dimness of vision became so marked that on several occasions while driving his automobile home from work, he had to stop for a few minutes until his vision cleared slightly before he could proceed further. At the time of examination he had ceased driving. Physical examination revealed a well developed white male, weight 207 lb. The skin showed slight pallor. The pupils reacted normally to light but more slowly to accommodation. Heart, lungs, and abdomen were normal. Reflexes were normal. Blood sugar tolerance analyses were as follows:

	Blood Sugar	*Urine Sugar*
Fasting	78 mg.	Slight
30 Min.	150 mg.	Moderate
1 Hr.	124 mg.	Large Amt.
2 Hr.	90 mg.	Slight
3 Hr.	74 Mg.	Slight

Case 5—I. H., a white male, age 44, had been exposed for 6 weeks before examination. He observed no symptoms until about 3 weeks after he began to work over the vats. He then began

to have nausea and headache but did not vomit until about 1 week later when the vomiting became very severe. At this time he was unable to retain any food in his stomach. The attacks of vomiting were accompanied by severe abdominal cramps. He also had attacks of diarrhea which varied in severity. He stated that for the past few nights he had been unable to sleep, although he felt sleepy and tired. During the period of exposure there had been a gradual but complete loss of sexual libido. During this period he lost 9 lb. in weight. Physical examination showed a well developed white male, weight 156 lb. The conjunctivae were congested and there was slight epiphora. Heart, lungs, abdomen and reflexes were normal. Blood sugar tolerance analyses were as follows:

	Blood Sugar	*Urine Sugar*
Fasting	96 mg.	None
30 Min.	124 mg.	Moderate
1 Hr.	116 mg.	Slight
2 Hr.	95 mg.	Slight
3 Hr.	90 mg.	Slight

Ophthalmoscopic examination in these cases did not reveal any abnormalities except a slight paleness of the disc. Toxic amblyopia being suspected, perimetric examinations of the five men were made. All of the men, including the two who had not suffered from visual disturbances, showed bilateral peripheral constriction of the color fields. No central scotomata were present in any of the perimetric charts. A B&L Stereo-Campimeter was employed in making all central field studies. Peripheral fields were checked up with a campigraph. Illumination in all cases and the size of the test object (1½°) were kept constant. A uniform procedure of examination was employed in all cases, targets being moved from non-visible to visible. Periodic observations in Case 1 illustrate the progress of a typical case. With the removal of exposure, the subjective visual disturbances as well as the general complaints disappeared. At intervals of 7 to 10 days, perimetric examinations were repeated, and revealed a gradual expansion of all the color fields which were found to be within normal limits 5 weeks after cessation of exposure.

PATHOLOGICAL PHYSIOLOGY

The pathological physiology of the toxic amblyopia observed in carbon tetrachloride intoxication appears to be closely associated with disturbances in carbohydrate and fat metabolism. Lamson [2] states that "carbon tetrachloride produces a liver necrosis with an increase of guanidine or guanidine-like substances in the blood with a subsequent fall of blood sugar." In this group of cases, the men had blood glucose concentrations which were at the lower border of the normal variation and, in some cases, even below this. Moreover, slight amounts of sugar were found in the fasting urine specimens and larger amounts after the administration of glucose, especially in Case 2. The blood sugars, urines, and the visual fields returned to normal after the men left their work and were put on a high calcium and dextrose diet. This therapy has been used in carbon tetrachloride poisoning by many investigators including Minot and Cutler.[3]

Recently, Adler [4] has demonstrated that that portion of vitreous humor of the eye which is in close contact with the retina contains less sugar than the more anterior layers. This was shown to be due to the fact that the retina has a greater glycolytic power than any other tissue of the eye, *i.e.*, the low sugar content of the vitreous is a result of the rapid utilization of glucose by the adjacent retina. All sugar entering the vitreous must first pass through the

retinal circulation, where a portion of it is consumed. Adler further demonstrated that sugar could not pass into the vitreous from the aqueous humor. He suggests that " possibly the retina, not having storage facilities for glycogen, is forced to use the glucose circulating in the blood for its metabolic need."

A lipemia and a cholesterolemia have been shown to be present in carbon tetrachloride poisoning as a result of central necrosis and fatty degeneration of the liver. MacMahon and Weiss [5] report an autopsy in a case of severe carbon tetrachloride poisoning in which the blood in the pulmonary arteries contained 64 per cent fat and in the inferior vena cava 25 per cent. They state that the source of the fat was the liver which showed severe injury. Butsch [6] reports a non-fatal case of carbon tetrachloride intoxication in which the blood fat on admission was 1,245 mg. per 100 c.c. estimated as tripalmitin, but which dropped to 765 mg. 3 weeks later. The serum cholesterol in this case was 856 mg. per 100 c.c. on admission and 563 mg. after 3 weeks. The patient was back at work 1 month after admission to the hospital.

According to Adler,[4] " there is clinical evidence that some substance present in the liver and in certain fats is concerned with rod-visual purple function." The periphery of the retina consists chiefly of rods, and, moreover, the visual purple is most abundant in this area. The scotomata which occur as a result of disturbances of the outer layer of the retina, which includes the rod-visual purple mechanism, correspond in " position, shape and extent to the retinal lesion."

Whatever theoretical explanation these facts may have, it is suggested that (a) as a result of the low blood sugar which is encountered in carbon tetrachloride intoxication, the retina is deprived of an adequate source of glucose, a constant supply of which is essential to the normal metabolism and function of the retina; (b) that another factor in the visual disturbance may be an alteration of the rod-visual purple mechanism of the periphery associated with the deranged fat metabolism.

Although the constitutional symptoms in the present series of cases were not especially severe, the constriction of the color fields was marked even in the mildest case. It is of utmost significance that carbon tetrachloride intoxication can be detected at an early stage by routine perimetric examination of exposed workers. It is probable that similar phenomena may be discovered by the same method in intoxications caused by other fat solvents, such as chloroform or benzol.

CONCLUSIONS

1. Toxic amblyopia may result from exposure to carbon tetrachloride vapor.

2. The resulting amblyopia is characterized by concentric constrictions of all the color fields without central scotomata.

3. The resulting amblyopia differs from the usual toxic amblyopia, of which that due to carbon bisulphide is typical, in that the color fields in the latter are marked by central scotomata with a normal periphery.

4. With cessation of exposure, and a high calcium and dextrose diet, the amblyopia rapidly disappear.

5. Routine examination of the visual fields of workers exposed to the vapor of carbon tetrachloride is suggested to detect intoxication at an early stage.

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